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PCT/KR2003/000445

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference NP-18981-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/000445**	International filing date *(day/month/year)* **07 MARCH 2003 (07.03.2003)**	Priority date *(day/month/year)*

International Patent Classification (IPC) or national classification and IPC

IPC7 A61K 31/133

Applicant

KOREA ATOMIC ENERGY RESEARCH INSTITUTE et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
08 SEPTEMBER 2004 (08.09.2004)	07 JUNE 2005 (07.06.2005)

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International aplication No.
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I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the claims:
pages _____ , as originally filed
pages _____ , as amended (together with any statment) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the drawings:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the sequence listing part of the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language English which is

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☒ the language of publication of the international application(under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/ or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained inthe international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-6	YES
	Claims		NO
Inventive step (IS)	Claims	1-6	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-6	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents are referred to in this report:

D1 : TATSUYA, SUGAWARA, et al., " Apoptosis Induction by Wheat-flour Sphingoid Bases in DLD-1 Human Colon Cancer Cells", Bioscience, Biotechnology, and Biochemistry, 2002, 66(10), pp.2228-31

D2 : NATZKER S., et al, " Cis-4-methylsphingosine phosphate induces apoptosis in neuroblastoma cells by opposite effects on p38 and ERK mitogen-activated protein kinases", Biological Chemistry, 2002, 383(12), pp.1885-94

D3 : SPIEGEL S., et al., "Sphingosine 1-phosphate as a therapeutic agent", Leukemia, 2002, 16(9), pp.1596-602

1. Novelty

The present invention relates to a composition for cancer treatment or enhancement of radiosensitizing effect comprising phytosphingosine or N-alkanoyl derivative thereof. D1, which is considered to represent the most relevant state of the art, discloses the apoptotic effects of wheat-flour sphingoid bases on human colorectal cancer cells. Also, the authors of D1 suggest that the reduction of cancer cell viability by sphingoid bases from wheat flour is mainly due to cis- and trans-8-sphingenine. D2 discloses that cis-4-methylsphingosine phosphate induces apoptosis in neuroblastoma cells. D3 discloses that changes in sphingosine-1-phosphate and ceramide have been implicated in a number of pathological conditions in which apoptosis plays an important role. None of the prior art cited in the search report discloses definitely a physiological role of phytosphingosine.

Therefore, the present invention is considered to be novel(PCT Article 33(2)).

(Continued on Supplemental Sheet.)

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The expression in the claim 1 "substituted" is non-limitative and is therefore not regarded as obvious modification or an equivalent of the examples which have been given in the description.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

2. Inventive Step

Even though D1 describes a composition of wheat-flour sphingoid base including 4-hydroxysphinganine(that is the same compound as phytosphingosine), it is not obvious to a skilled person in the art to select 4-hydroxysphinganine for an active ingredient of an anti-cancer composition with the disclosure in D1 that the apoptosis effect of wheat-flour sphingoid bases is mainly due to cis- and trans-8-sphingenine.

Therefore, an inventive step can be acknowledged for the present invention(PCT Article 33(3)).

3. Industrial Applicability

The present invention is considered to be industrially applicable(PCT 33(4)).